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Original Article

Efficacy and safety of intralesional vitamin D3 injection in wart

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ABSTRACT

Background: Verrucae, or warts, are the benign proliferations of mucosa and skin. They present over the hands in most patients but can occur anywhere on the surface of the skin or the mucosa.**Aim:** To investigate both the safety and effectiveness of intralesional cholecalciferol (vitamin D3) in the management of warts.**Materials and Methods:** This observational study included 40 patients with cutaneous warts, conducted from April 2023 to April 2024 at the Alirada clinic. After administering lignocaine (0.2 mL, 20 mg/mL), vitamin D3 (0.2 mL, 15 mg/mL) was injected into the base of the warts. Injections were repeated every two weeks for a maximum of four sessions or until complete resolution **Results:** The mean age was 30.85 ± 12.51 years, with a mean wart duration of 15.75 ± 12.15 months and an average of 7.8 ± 6.7 warts per patient. The group comprised 45% males and 55% females. Wart types included: filiform (5%), palmoplantar (70%), plane (10%), and verruca vulgaris (15%). Complete resolution occurred in 65% of cases, moderate response in 15%, mild response in 15%, and no response in 5%. At baseline, 10 patients (25%) reported pain due to the warts, primarily in palmoplantar warts, with 90% resolution within 14 days of treatment. After treatment, post-injection pain occurred in 12 patients (30%), mostly transient and resolving within 3–5 days. Other side effects included swelling (20%), nodule formation (7.5%), and pigmentary changes (hyper- or hypo-) (2.5%), with no hypopigmentation reported. Treatment response was positively correlated with gender and verruca vulgaris but negatively correlated with plane warts**Conclusion:** Intralesional vitamin D3 treatment is simple, effective, affordable, safe, and easy to administer in outpatient clinics. However, small sample sizes limit generalizability for certain wart types.

Key words: Warts; Vitamin D3; Skin.

Introduction

Verrucae, or warts, are the benign proliferations of mucosa and skin. They present over the hands in most patients but can occur anywhere on the surface of the skin or the mucosa [1].

The causative agent of warts is the human papillomavirus (HPV). The DNA viruses are diverse, with about 100 different genotypes. Most routes of HPV infection are spread either directly by contact with an infected person or indirectly by contact with a contaminated surface or object [2]. The basal keratinocytes of the epidermis are the main target of HPV infections. These cells can become infected through small cuts or scrapes, and the infection is made worse by roughening up the epithelium [3].

Warts are a prevalent medical condition that affects roughly 10% of the population. As high as 10% to 20% of school-aged children are affected. Immunocompromised patients and meat handlers are also at higher risk. Warts arise at any age [4].

Usually, damaging therapies like electrocoagulation, cryotherapy, topical 5-fluorouracil, laser, or topical salicylic acid are used to treat or remove warts. In essence, every one mentioned therapy are time-consuming, commonly recurrent, and painful [5].

None of these therapy options is regarded as the gold standard, and they may be time-consuming, expensive, and/or painful. Within sixty-five percent to seventy-eight percent of cases, resolution may occur within 2 years of treating the wart [6].

Consequently, in an effort to deal with these deficiencies, immune treatment was extensively investigated in the past few decades as a treatment for warts. This treatment acts on the basic principle of improving cell-mediated immunity[7].

A variable degree of success was observed in the treatment of warts with topical vitamin D. Vit D regulates cell differentiation and proliferation and possesses immunoregulatory properties. vitamin D impacts are mediated by the vitamin D receptor (VDR), that can be found in fibroblasts, melanocytes, keratinocytes, and immune system cells of the skin[8].

The aim of this research was to explore the safety and effectiveness of intralesional cholecalciferol for warts treatment.

Materials and Methods

This was an observational study performed on 40 cases from April 2023 to April 2024 at the Alirada clinic. The

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investigation focused on all consecutive cases, both women and men, who had cutaneous warts and had not received previous therapy using topical or destructive modalities for a minimum of six months.

Inclusion criteria: cases with various sizes and periods of multiple or single warts, with or without distant warts.

Exclusion criteria: cases with acute febrile illness, those who were given wart therapy prior to research enrollment, lactating and pregnant females; patients <12 and >70 years of age; those with allergies or hypersensitivity to vitamin D3, cases with immunoinhibition or other systemic or skin-related illnesses; and cases with a history of kidney disease or with hypercalcemia.

All cases with warts have been diagnosed by history and clinical characteristics. The study used a standardized questionnaire to collect information about each patient, including age, gender, warts number, illness duration, place, size, prior history and family history, and absence or presence of remote warts. Pain assessment included baseline wart-related pain (reported as a primary complaint, particularly for palmoplantar warts due to their location on weight-bearing surfaces) and post-injection pain as an adverse event. Both were recorded via patient self-reports and clinical evaluations at baseline and during follow-up visits**.** Each patient received a personalized graphical wart map. Photographs were collected throughout each visit to complement reported data. The clinical response has been shown by the reduction in the number and size of warty lesions.

Vitamin D3 injection administration and dosage

The base of the wart was administered with approximately 0.2 milliliters of vitamin D3 solution (6,00,000 IU, fifteen milligrams per milliliter) following the injection of lignocaine (0.2 milliliter, twenty milligrams per milliliter). A maximum of 4 warts have been administered per session at two-week intervals till resolution or a maximum of 4 injections occurred. A clinical examination of the results was conducted on cases at two-week intervals. For identifying any recurrences, cases have been monitored for a period of six months following the final administration.

The degree of decrease in the warts number and size was evaluated by comparing before and after intervention photographs (with before images presented first followed by after images as per standard medical practice). The response to therapy has been assessed in the following manner: The total resolution of warts has been described as complete resolution (CR). The clinician and photographic examination evaluated partial response as a reduction in number and/or apparent size. Additionally, the resolution of distant, unmanaged warts has been evaluated.

Monitoring duration evaluation: Dermoscopy and colored photographs were utilized to assess the degree of enhancement during the two-month therapy period. An additional six months of monitoring without therapy were conducted at every-month intervals to identify any recurrences. The clinical response has been recorded by documenting the reduction in the number and size of warty lesions at every checkup, which occurred at two-weekly intervals for four sessions and six months following the final injection. Complete resolution has been defined as the complete resolution of all warts, including those that were managed and those that were distant. A mild response has been defined as a decrease in both the number and size of lesions of one percent to less than fifty percent, while a moderate response has been defined as a decrease in fifty to less than one hundred percent [9]**.** The cases have been told to keep away from using any topical or oral drugs following their therapy.

Ethical considerations: All the procedures of the research were approved by the ethics committee of Faculty of Medicine, Internal Medicine department, Elmergib University, Libya. Administrative consents required were taken. The purpose of this study was to perform research on humans in compliance with the Declaration of Helsinki, the code of ethics of the World Medical Association.

Statistical Analysis

The degree of association between the therapy's response as well as additional parameters has been estimated using Spearman's correlation. A P value of less than.05 has been regarded as statistically significant. Given the small sample sizes for certain wart subtypes, statistical power calculations were limited, and results should be interpreted with caution for subgroups with fewer than 10 cases.

Results

According to Table 1, mean age (years) was 30.85±12.51, mean duration of wart (month) was 15.75±12.15, mean number of warts was 7.8±6.7, and 45% of the studied group were male and 55% were female.

Table 1: Distribution of demographic data in the studied group.

	Studied group N=40	
	Mean	**±SD**
Age (years)	30.85	12.51
Duration of wart (month)	15.75	12.15

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Number of warts	7.8	6.7
	N	%
Sex		
Men	18	45%
Women	22	55%

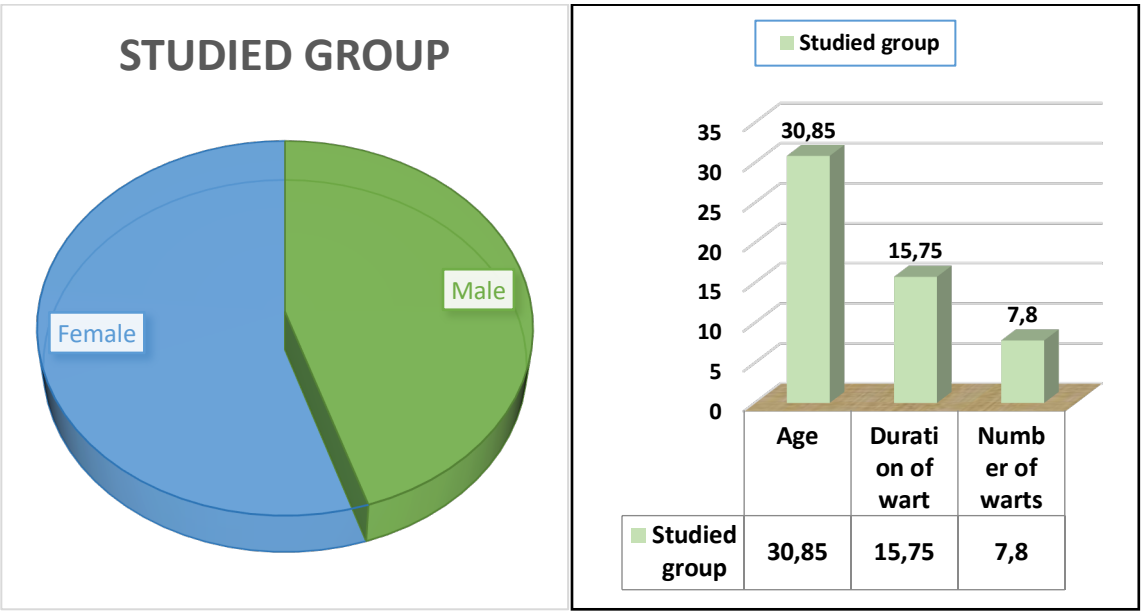
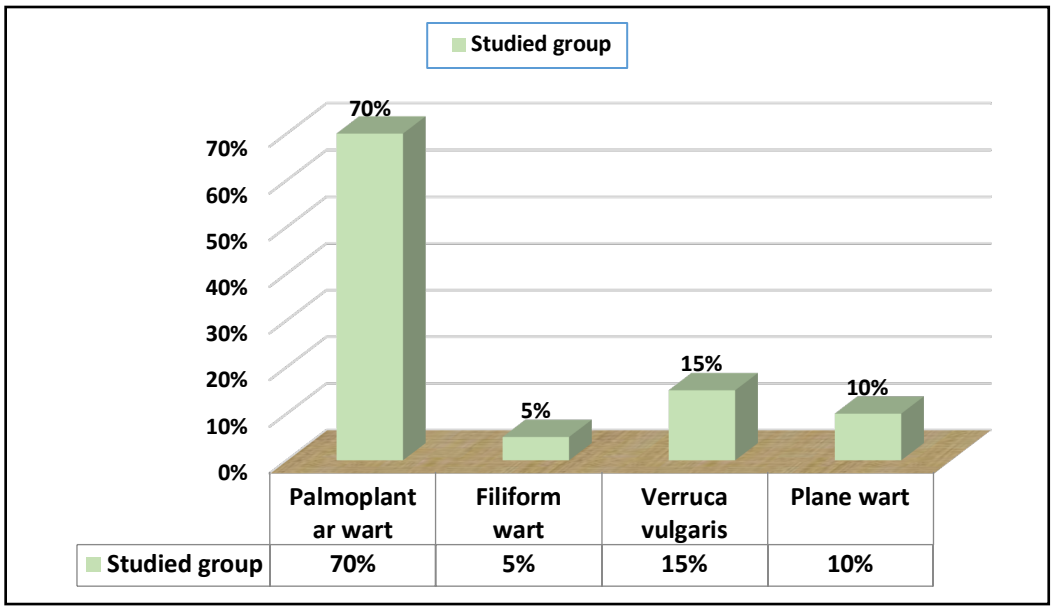


Figure 1: Distribution of demographic data in the studied group.

According to Table 2: Wart types included filiform (5%), palmoplantar (70%), plane (10%), and verruca vulgaris (15%).

Table 2: Distribution of types of warts in the examined group.



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	Studied group N=40	
	N	%
Palmoplantar wart	28	70%
Filiform wart	2	5%
Verruca vulgaris	6	15%
Plane wart	4	10%

Figure 2: Distribution of types of warts in the studied group.

Table 3 showed that, treatment outcomes showed 65% complete resolution 15 % moderate response, 15% mild response, and 5% no response.

Table 3: Distribution of treatment response in the studied group.

	Studied group N=40	
	N	%
Complete resolution	26	65%
Moderate	6	15%
Mild	6	15%
No response	2	5%

Figure 3: (A) Before treatment (no response); (B) After treatment (complete resolution in palmoplantar warts).

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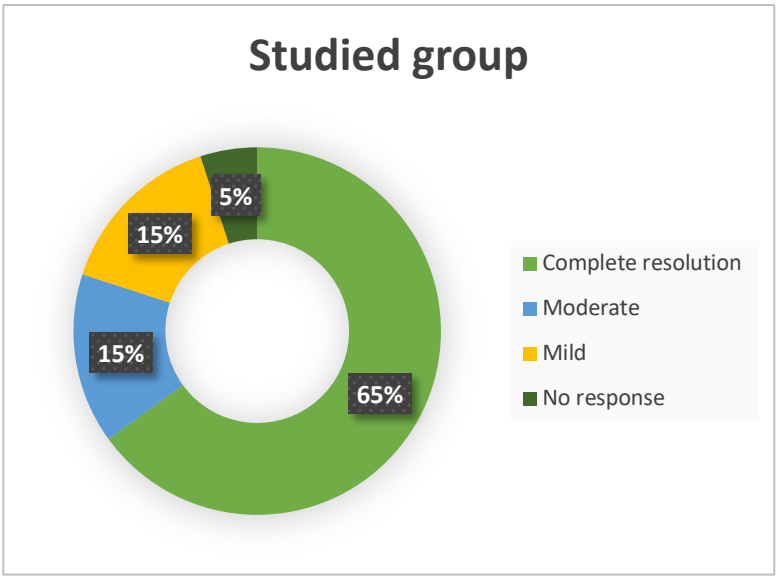

Figure 4: Distribution of treatment response in the studied group.

Table 4 showed that, the palmoplantar wart group (N=28) had the highest success rate, with 20 patients (71.4%) achieving complete resolution and 1 (3.6%) showing no response. The filiform wart group (N=2) had 50% complete resolution and 50% moderate response. Verruca vulgaris cases (N=6) showed 50% complete resolution, with the remainder split equally among moderate, mild, and no response (16.7% each). The plane wart group (N=4) had 2 patients (50%) with complete resolution and 2 (50%) with moderate response, with no non-responders

Table 4: Treatment response according to type of wart

	Palm-plantar wart N=28	Filiform wart N=2	Verruca vulgaris N=6	Plane wart N=4
Complete resolution	20 (71.4%)	1 (50%)	3 (50%)	2 (50%)
Moderate	3 (10.7%)	1 (50%)	1 (16.7%)	2 (50%)
Mild	4 (14.3%)	0 (0%)	1 (16.7%)	0 (0%)
No response	1 (3.6%)	0 (0%)	1 (16.7%)	0 (0%)

Table 5 showed that, regarding side effects observed in the studied group, the most commonly reported adverse effect was post-injection pain (12 patients, 30%), followed by swelling (8 patients, 20%), and nodule formation (3 patients, 7.5%). Baseline wart pain (10 patients, 25%) and pigmentary changes (1 patient, 2.5%) were also noted, all of which resolved spontaneously without sequelae

Table 5: Distribution of Adverse Events and Baseline Complaints

	Studied group. N=40		
	N	%	Duration/Notes
Baseline wart pain	10	25%	**Primarily in palmoplantar warts due to weight-bearing surfaces; resolved in 90% within 14 days**

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Post-injection pain	12	30%	**Transient; resolved within 3–5 days**
Swelling	8	20%	Resolved in 75% of cases.
Nodule formation	3	7.5%	**Subsided spontaneously within 4 weeks without additional intervention**
Hyperpigmentation	1	2.5%	**Hyperpigmentation in one case;**
Hypopigmentation	0	0%	**no hypopigmentation**

Note: Baseline wart pain was reported primarily in palmoplantar warts due to their location on weight-bearing surfaces. Post-injection pain was transient, resolving within 3–5 days.

Table 6 showed that, among the studied group (N = 40), most adverse effects resolved spontaneously. Baseline wart pain improved in 9 patients (90%), post-injection pain in 11 patients (91.7%), swelling in 6 patients (75%), and all nodules (3 patients, 100%) subsided completely without intervention.

Table 6: Treatment Response by Adverse Events and Baseline Complaints

	Studied group N=40	
	Improved N %	**No Improvement %**
Baseline wart pain	9(90%)	1 (10%)
Post-injection pain	11 (91.7)	1 (8.3%)
Swelling	6 (75%)	2 (25%)
Nodule formation	3(100%)	0(0%)

Note: Baseline wart pain resolved within 14 days of treatment in most cases. Post-injection pain resolved within 3–5 days. Nodules resolved spontaneously without additional treatment.

Pain Assessment Results: At baseline, 10 patients (25%) reported pain due to the warts, primarily associated with palmoplantar warts due to their location on weight-bearing surfaces, with 90% resolution within 14 days of treatment. Post-injection pain occurred in 12 patients (30%), mostly transient and resolving within 3–5 days.

According to table 7, pain was the most frequently reported side effect among patients (N=12), with a high response rate of 11 patients (91.7%) showing improvement, and only 1 patient (8.3%) exhibiting no response. Swelling (N=8) showed a lower response rate, with 6 patients (75%) responding to treatment, while 2 patients (25%) showed no improvement. Notably, nodule formation (N=3) demonstrated the best outcome, with all patients (100%) responding positively and no cases of non-response reported.

Table 7: Treatment response according to type of wart

	Pain N=12	**Swelling N=8**	**Nodule formation N=3**
Response	11 (91.7%)	6 (75.0%)	3 (100.0%)
No response	1 (8.3%)	2 (25.0%)	0 (0.0%)

According to table 8, a significant positive correlation was discovered among the responses of the management and gender and Verruca vulgaris, while an insignificant correlation was discovered among the responses of the management and plane wart.

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Table 8: Association among response of the management and additional parameters in the studied group.

	Response of the treatment	
	r	P-value
Age	0.03	0.82
Gender	0.37*	0.01
Duration of wart	-0.14	0.37
Number of warts	-0.12	0.43
Palmoplantar wart	-0.21	0.17
Filiform wart	-0.02	0.87
Verruca vulgaris	0.47**	0.002
Plane wart	-0.036	0.03

r= Pearson Correlation,

DISCUSSION

Warts are benign and common proliferations of the skin and mucosa caused by the human papillomavirus (HPV). More than 100 distinct HPV genotypes have been identified. Warts often cause significant discomfort and social embarrassment [10]. Immunotherapy enhances the host immune response against HPV, promoting lesion clearance without the need for destructive procedures or scarring [11]. Intralesional vitamin D3 is believed to exert its therapeutic effect by regulating epidermal cell proliferation and differentiation, modulating cytokine production, and upregulating vitamin D receptors and antimicrobial peptides such as cathelicidin (LL-37) in the skin [12]. Through these mechanisms, vitamin D3 strengthens the immune response against HPV, leading to wart resolution without scarring.

This study demonstrated a 65% complete resolution rate, with palmoplantar warts showing the highest success (71.4%). These results are consistent[19], who reported a 72.6% complete resolution rate in 62 patients with plantar warts, [16], who observed 65% complete clearance in 40 patients. Similarly,[14] reported 70% clearance in 20 plantar wart cases,[15]. achieved 82.6% resolution in palmoplantar warts. Minor variations in clearance rates among studies may be due to differences in dosing regimens (e.g., 0.2 mL of 15 mg/mL in our study vs. other concentrations), injection intervals (biweekly in our study), wart types, or follow-up durations (three months vs. longer follow-up in other studies).

Adverse effects were mild and transient, with post-injection pain (30%), swelling (20%), and nodule formation (7.5%) being the most frequent. All nodules resolved spontaneously within four weeks without intervention. Baseline wart-related pain was reported by 10 patients (25%), predominantly in palmoplantar lesions due to their weight-bearing location, and resolved in 90% of cases within 14 days, concurrent with wart resolution. Post-injection pain was reported by 12 patients (30%) and was transient, resolving in 91.7% of cases within 3–5 days. Pigmentary changes (hyper- or hypopigmentation) occurred in only one patient (2.5%), with no hypopigmentation observed. Compared with cryotherapy, which may cause scarring or pigmentary alterations, intralesional vitamin D3 showed a superior safety profile, consistent[14,15].

The study population had a mean age of 30.85 ± 12.51 years, comprising 55% females and 45% males. The predominant wart type was palmoplantar (70%), followed by verruca vulgaris (15%), plane warts (10%), and filiform warts (5%). A positive correlation was observed between treatment response and male gender as well as verruca vulgaris, whereas a negative correlation was seen with plane warts. These findings are consistent [13,14].

Palmoplantar warts are often painful due to their location on weight-bearing surfaces. Among the 12 patients who experienced post-injection pain, 11 (91.7%) showed marked improvement within 3–5 days. However, the study did not systematically record the number of sessions required for the relief of baseline wart pain, which represents a limitation for future studies. The superior response in males and in verruca vulgaris may reflect differences in local immune response or wart morphology (e.g., vascularity, thickness), warranting further investigation.

Our results are in agreement with[13], who found a significant association between male gender and favorable outcomes after vitamin D3 therapy,[14]. Observed a similar correlation (P = 0.047). No significant associations

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were found with age, wart duration, or number of warts, consistent [17], reported no such correlations (P > 0.05).

Limitation

However, it is important to acknowledge several limitations of our study. The sample size was relatively small (n=40), and certain wart subtypes had particularly limited representation: filiform warts (n=2), plane warts (n=4), and verruca vulgaris (n=6). These small subgroup sizes significantly limit the statistical power and generalizability of our findings for these specific wart types. Drawing definitive conclusions about treatment efficacy based on only 2 cases of filiform warts or 4 cases of plane warts may lead to overestimation of results and should be interpreted with caution. Additionally, the timeline for pain relief in palmoplantar warts was not systematically documented, representing a key limitation. Future studies with larger, more balanced sample sizes across all wart subtypes would be necessary to validate these preliminary findings.

Conclusion

Intralesional vitamin D3 is a simple, safe, affordable, and effective outpatient treatment, particularly for palmoplantar warts (71.4% complete resolution). Baseline wart pain (25%) and post-injection pain (30%) were well-managed, with 90% and 91.7% improvement rates, respectively. Other side effects, including swelling (75% improvement) and nodule formation (100% spontaneous resolution), were well-tolerated, with minimal post-treatment hyperpigmentation (2.5%). However, small sample sizes for certain wart types, lack of pain relief timeline data, and the absence of a control group limit generalizability. Future multicenter randomized controlled trials with larger, balanced samples are needed to validate these findings.

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